

As used herein and in the claims, the term "animal" refers to any organism with an immune system.

According to yet another aspect of the present invention there is provided a pharmaceutical composition for inducing protective immunity against multiple sclerosis. The composition comprises a pharmaceutically acceptable carrier and an antibody being capable of binding an interferon gamma inducing factor.

Alternatively, the composition according to the present invention comprises a pharmaceutically acceptable carrier and an interferon gamma inducing factor or an immunogenic portion thereof, thereby eliciting an antibody being capable of binding the interferon gamma inducing factor *in vivo*.

As used herein the phrase "immunogenic portion" refers to an immunogenic proteinaceous compound, which may include, among optional additional components, a plurality of amino acid residues. The term "amino acid" is understood to include the 20 naturally occurring amino acid residues; those amino acid residues often modified post-translationally *in vivo*, including for example hydroxyproline, phosphoserine and phosphothreonine; and other unusual amino acid residues including, but not limited to, 2-aminoadipic acid, hydroxylysine, isodesmosine, nor-valine, nor-leucine and ornithine. Furthermore, the term "amino acid" includes both D- and L-amino acid residues. The amino acid residues according to the present invention form a peptide. The latter is understood to include native peptides, including degradation products or synthetically synthesized peptides, and further to peptidomimetics, such as peptoids and semipeptoids, which are peptide analogs, which may have, for example, modifications rendering the peptides more stable or less immunogenic while contacting body fluids. Such modifications include, but are not limited to, cyclization, N terminus modification, C terminus modification, peptide bond modification, including, but not limited to, $\text{CH}_2\text{-NH}$, $\text{CH}_2\text{-S}$, $\text{CH}_2\text{-S=O}$, O=C-NH , $\text{CH}_2\text{-O}$, $\text{CH}_2\text{-CH}_2$, S=C-NH , CH=CH or CF=CH , backbone modification and residue modification. Methods for preparing peptidomimetic compounds are well known in the art and are specified in Quantitative Drug Design, C.A. Ramsden Gd., Chapter 17.2, F. Choplin Pergamon Press (1992), which is incorporated by reference as if fully set forth herein.

According to yet additional aspect of the present invention there is provided a method for treating an animal for inducing protective immunity

against multiple sclerosis. The method is effected by administering, to the animal, an antibody capable of *in vivo* neutralizing an interferon gamma inducing factor in affecting cells to produce interferon gamma.

According to still additional aspect of the present invention there is provided a method for treating an animal for inducing protective immunity against multiple sclerosis. The method is effected administering, to the animal, an antigen including an interferon gamma inducing factor or an immunogenic portion thereof, thereby eliciting an antibody being capable of binding *in vivo* an interferon gamma inducing factor.

As used herein the term "antigen" refers to an immunogen including at least one immunogenic epitope, which is represented in the equivalent native peptide in a continuous or discontinuous fashion.

According to a preferred embodiment of the present invention, the antibody is polyclonal. Preparation of polyclonal antibodies is known in the art and further described in the Examples section hereinafter.

According to another preferred embodiment of the present invention, the antibody is monoclonal. Methods of producing and identifying monoclonal antibodies are well known in the art.

Monoclonal antibodies may be obtained by processes comprising the generation of a plurality of monoclonal antibodies to an antigen and screening the plurality of antibodies so generated to identify a monoclonal antibody that binds and/or neutralizes the peptide of interest, interferon gamma inducing factor in the present case. Monoclonal antibodies may be generated either *in vitro* or *in vivo*. In a related process, an animal is immunized with an antigen thereby generating antibody producing lymphocytes in said animal, antibody producing lymphocytes are removed from the animal, said lymphocytes are fused with myeloma cells to produce a plurality of immortalized hybridoma cells each of which produces monoclonal antibodies, the plurality of monoclonal antibodies is screened to identify a monoclonal antibody that binds the peptide, and the hybridoma producing the antibody is cloned and propagated. Animals are typically immunized with a mixture comprising a solution of the immunogen in a physiologically acceptable vehicle, and any suitable adjuvant, which achieves an enhanced immune response to the immunogen. By way of example, the primary immunization conveniently may be accomplished with a mixture of a solution of the immunogen and Freund's complete adjuvant, said mixture being prepared in the form of a water in oil emulsion. Typically the immunization may be administered to the animals

intramuscularly, intradermally, subcutaneously, intraperitoneally, into the footpads, or by any appropriate route of administration. The immunization schedule of the immunogen may be adapted as required, but customarily involves several subsequent or secondary immunizations using a milder adjuvant such as Freund's incomplete adjuvant. Antibody titers and specificity of binding to the hapten can be determined during the immunization schedule by any convenient method including by way of example radioimmunoassay, or enzyme linked immunoassay. Antibody activity assays can be performed in vitro as further exemplified in the Examples section that follows. When suitable antibody titers are achieved, antibody producing lymphocytes from the immunized animals are obtained, and these are cultured, selected and cloned, as is known in the art. Typically, lymphocytes may be obtained in large numbers from the spleens of immunized animals, but they may also be retrieved from the circulation, the lymph nodes or other lymphoid organs. Lymphocytes are then fused with any suitable myeloma cell line, to yield hybridomas, as is well known in the art. Alternatively, lymphocytes may also be stimulated to grow in culture, and may be immortalized by methods known in the art including the exposure of these lymphocytes to a virus, a chemical or a nucleic acid such as an oncogene, according to established protocols. After fusion, the hybridomas are cultured under suitable culture conditions, for example in multiwell plates, and the culture supernatants are screened to identify cultures containing antibodies that recognize the hapten of choice. Hybridomas that secrete antibodies that recognize the hapten of choice are cloned by limiting dilution and expanded, under appropriate culture conditions. Monoclonal antibodies are purified and characterized in terms of immunoglobulin type binding affinity and in vivo or in vitro neutralizing activity.

The antibody according to the present invention, be it a poly- or monoclonal antibody, is a neutralizing antibody to interferon gamma inducing factor in affecting cells to produce interferon gamma, that is to say that the antibody interferes with the functionality of interferon gamma inducing factor in affecting cells to produce interferon gamma.

According to an additional aspect of the present invention there is provided a method for treating an animal for inducing protective immunity against multiple sclerosis. The method according to the present invention is effected by administering, to the animal, cells capable of producing and secreting an antibody capable of *in vivo* neutralizing an interferon gamma